

PATENT SPECIFICATION

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(54) DENTAL CARE PREPARATIONS

(71) We, ED. GEISLICH SOHNE
 A.G. FÜR CHEMISCHE INDUSTRIE, a
 Swiss Body Corporate of Wolhusen, Lucerne,
 Switzerland, do hereby declare the invention,
 for which we pray that a patent may be
 granted to us, and the method by which it
 is to be performed, to be particularly de-
 scribed in and by the following statement:—

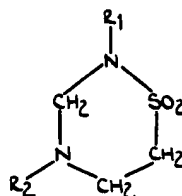
This invention relates to novel preparations
 for the treatment of tooth and gum infections
 and in particular parodontosis.

Paradontosis is a progressive, chronic in-
 flammatory infection of the immediate sur-
 roundings of the tooth root and the tooth bed
 (parodontium). This disease, which is increas-
 ingly common in men and women over 30
 years of age, successively establishes itself in
 the gingival border, the periodontal mem-
 brane and the osseous tooth socket.

A healthy gum lies firmly around the neck
 of the tooth, but when circulation disorders
 occur, it becomes flaccid, tends to bleed and
 loosens itself from the tooth, producing a
 gingival pocket.

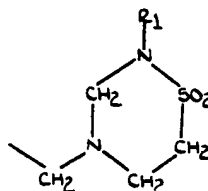
Paradontosis is caused by a bacteria and
 their metabolic products and it is associated
 with the build up of tartar and bacterial
 plaque. We have now found that, although
 dental care preparations have commonly
 contained bactericides for many years, without
 affording significant protection against para-
 dontosis, one particular class of bactericides
 is very effective. We believe that this effec-
 tiveness is due to the unique action of the
 compounds concerned not only against the
 bacteria but also against the toxins produced
 by the bacteria.

The class of bactericides which we have
 found to be effective against paradontosis
 are the formaldehyde carriers, that is non-
 toxic compounds containing formaldehyde in
 combination, which are capable of producing
 formaldehyde at the site of action. British
 Patent Specification No. 1,124,285 discloses
 and claims one class of such compounds, in-
 cluding *inter alia* compounds of general formula



I

in which R₁ is hydrogen or a straight or
 branched alkyl group having 1—6 carbon
 atoms, for example a methyl, ethyl, propyl,
 isopropyl, butyl, isobutyl, amyl or hexyl group
 and R₂ is hydrogen or a group of the formula



(wherein R₁ is as defined above).

Thus according to one feature of the pre-
 sent invention there is provided a dental care
 preparation for the treatment and/or prophyl-
 axis of paradontosis in the form of a tooth-
 paste, toothgel or mouthwash as herein de-
 fined comprising, as active ingredient, at
 least one compound of formula I (as herein-
 before defined).

The expression "toothpaste, toothgel or
 mouthwash" is used herein to designate pre-
 parations of an orally acceptable nature con-
 taining carriers and excipients conventionally
 used for such purposes, with the proviso that
 it does not include solvents together with the
 active ingredient of formula I which give
 rise to more known solutions or suspensions.

We have found, however, that the com-
 pound of choice is bis - (1,1 - dioxo - per-
 hydro - 1,2,4 - thiadiazinyl - 4) - methane
 (also referred to herein as Taurolin) in view
 of its extremely low toxicity when given
 over long periods. On the other hand, com-
 pounds in which R₁ is alkyl tend to have en-

hanced affinity for the gum which improves their effectiveness.

As indicated, the production of this compound and of the other compounds of formula I is described in British Patent Specification No. 1,124,285.

It is noteworthy that the formaldehyde carriers of formula I are effective in treatment of paradontosis, while chlorhexidine, which has been previously suggested for treatment of paradontosis, is not active against the bacterial toxins and is consequently incapable of complete treatment of the disease. Furthermore, the chlorhexidine digluconate solutions which have previously been used have the disadvantage of causing yellowness of the teeth and further have an unpleasant bitter taste. In addition, chlorhexidine is known to produce p-chloroaniline, a very toxic substance, on degradation, so that it is not suitable for long-term treatment of mouth conditions.

In general, the concentration of the active substance in dental care preparations will be higher in the therapeutic treatment of an established paradontosis than in the prophylactic treatment of the teeth to prevent such disease. For therapeutic purposes, the dental care preparations should contain 1—3% by weight, preferably about 2% by weight, of the active material, while for prophylaxis, the preparations should contain 0.5—1.5% by weight of active material, preferably about 1% by weight.

The dental care preparations into which the active material of formula I will be incorporated are toothpastes, both of the foaming and non-foaming types, tooth gels and mouth washes.

A toothpaste according to the invention may be of conventional composition and may, therefore, contain such ingredients as thickening or binding agents, humectants foaming agents, cleansing agents, preservatives, sweetening agents, flavouring agents and/or water.

Thickening or binding agents will in general be hydrophilic colloids of relatively high viscosity so as to give a creamy consistency to the paste and may, for example, be substances such as carboxymethylcellulose, methylcellulose, alginates, caragheenins, hydroxyethylcellulose, polyvinylpyrrolidone or silicic acid. In general, the quantity of binding or thickening agents will be widely variable, according to the nature of the other components and may vary from 1% up to 30% by weight or more.

Humectants may be such compounds as glycerol, sorbitol or propylene glycol; these substances may constitute a relatively large proportion of the composition, for example 10—30% by weight.

Preservatives which may be present include such substances as hydroxybenzoic acid esters. Sweetening agents include such sub-

stances as saccharine or sodium cyclamate. Flavouring agents include various aromatic oils, for example the traditional mint flavour oils.

The cleansing agent will, in general, be a very fine crystalline powder capable of producing light abrasion. The most suitable substance is calcium phosphate dihydrate, but other substances may be used including calcium carbonate, calcium pyrophosphate, aluminium hydroxide, aluminium oxide, calcium lactate, magnesium oxide, magnesium carbonate and precipitated silica.

In general, a relatively small quantity of surface active material will be present to assist cleansing of the teeth, even when the toothpaste is not intended to foam. A wide variety of surfactants are available. One particularly suitable class are polyoxyethylene derivatives of sugar alcohol mono-esters, such as polyoxyethylene sorbitan monolaurate and monostearate. Another product of this type is the polyoxyethylene derivative of castor oil sold under the trade name "Cremophor" EL (registered Trade Mark). It will be appreciated, however, that a very wide range of similar materials may be selected from the conventional surfactants available. In general, a non-ionic surfactant is preferred. In non-foaming preparations, the quantity of such non-ionic surfactants will be of the order of 0.5—1.5% by weight.

Where a foaming toothpaste is required, it is preferred to incorporate an anionic surfactant, such as a long-chain sulphate or sulphionate salt, for example sodium lauryl sulphate. These substances may, for example, be present at a level of 1—3%, e.g. about 2% by weight.

The water present is preferably deionised, to avoid problems in formulation.

It will be appreciated that many variants in the toothpaste formulations according to the invention are possible and the foregoing is not intended as an exhaustive list of the components which are possible.

Tooth gels will, in general, be very closely similar to toothpaste but will lack the abrasive tooth cleaning material and will thus generally be relatively optically clear. A medically acceptable dye will commonly be present in such formulations.

Mouth washes according to the invention may, again, be of the conventional type and may contain, for example, sweetening and flavouring agents, surfactants and/or, commonly, ethanol. Surfactants which may be present include non-ionic surfactants such as the polyoxyethylene derivatives mentioned above in relation to toothpastes, as well as the anionic surfactants also mentioned above. In general, mouth washes will be used therapeutically and will therefore contain the active material at the higher level as mentioned above.

Preparations according to the invention may, if desired, contain at least one further pharmacologically active ingredient such as, for example, a substance active against the formation of bacterial plaque, for example sodium benzoate, high molecular polyphosphates, sodium metaphosphate, magnesium tartrate, polyvinylpyrrolidone, polysiloxanes or sodium sulphuricinate. Similarly, preparations may contain substances active against caries, for example fluorine compounds.

The following Examples are given by way of illustration only. In the Examples, all percentages are percentages by weight.

- 15 Example 1
 Tooth gel
- 21.0% "Sident" 3 (registered Trade Mark)
(Silicic acid: Degussa)
- 29.0% Glycerine
- 20 28.0% Karion F liquid (70% Sorbitol
 solution. E. Merck, Darmstadt)
- 13.0% Propylene glycol
- 3.75% Water (deionised)
- 0.05% Saccharine (pure)
- 25 1.0% Taurolin
- 0.4% "Tween" 20 (registered Trade
Mark) (Polyoxethylen-Sorbitan-mono-
laurate: Atlas)
- 0.8% "Tween" 60 (Polyoxethylen-
Sorbitan-monostearate: Atlas)
- 30 1.0% Oleum menthae
- 2.0% "Texapon" K12 (registered Trade
Mark) (Sodiumlauryl salate: Henkel/
Dehydag)
- 35 Example 2
 Tooth gel, foaming
- 2.0% "Texapon" K12
- 1.0% Taurolin
- 1.5% Natrosol HR 250 (Hydroxyethyl-
Cellulose: Hercules Powder)
- 40 10.0% Kollidon 30 or 17 (Polyvinyl-
pyrrolidone: BASF)
- 0.5% Carmoisine B (Fast Red E) C.I.
16045 (Red Dye)
- 45 82.8% Water (deionised)
- 0.5% Saccharine 10% Solution
- 0.8% "Tween" 60
- 0.4% "Tween" 20
- 0.5% Oleum menthae
- 50 Example 3
 Tooth gel, non-foaming
- 1.0% Taurolin
- 1.5% Natrosol HR 250
- 10.0% Kollidon 30 or 17
- 55 0.5% Carmoisine B (Fast Red E) C.I.
16045
- 3.0% "Cremophor" EL (Castor-oil-
ethyleneoxide adduct: BASF)
- 0.5% Oleum menthae
- 60 1.0% Ethanol
- 0.5% Saccharine 10% solution
- 82.0% Water (deionised)

- Example 4
Tooth gel, non-foaming
- 1.0% "Carbopol" 934 (registered Trade
Mark) (Acrylic acid polymer: B. F.
Goodrich)
- 5.0% Kollidon 30 or 17
- 1.0% Taurolin
- 0.3% Carmoisine B (Fast Red E) C.I.
16045
- 70 90.5% Water (deionised)
- 0.5% Saccharine 10% solution
- 0.5% Oleum menthae
- 0.8% "Tween" 60
- 75 0.4% "Tween" 20
- pH adjusted to 7 with Triethanolamine.

- Example 5
Tooth gel, non-foaming
- 1.0% "Carbopol" 940
- 80 5.0% Kollidon 30 or 17
- 1.0% Taurolin
- 0.5% Carmoisine B (Fast Red E) C.I.
16045
- 88.5% Water (deionised)
- 85 0.5% Saccharine 10% solution
- 0.5% Oleum menthae
- 3.0% Cremophor EL
- Example 6
Tooth gel, non-foaming
- 90 1.0% Taurolin
- 1.5% Natrosol HR 250
- 10.0% Kollidon 30
- 0.5% Carmoisine B (Fast Red E) C.I.
16045
- 95 0.5% Oleum menthae
- 2.0% Ethanol
- 4.0% Saccharine 10% solution
- 1.0% "Cremophor" EL (Castor-oil with
Aethylenoxid-Product: BASF)
- 100 79.5% Water (deionised)

- Example 7
Tooth gel, non-foaming
- 1.0% "Carbopol" 941
- 105 5.0% Kollidon 30 or 17
- 1.0% Taurolin
- 0.5% Carmoisine B (Fast Red E) C.I.
16045
- 90.3% Water (deionised)
- 0.5% Oleum menthae
- 110 9.8% "Tween" 60
- 0.4% "Tween" 20
- 0.5% Saccharine 10% solution

- Example 8
Toothpaste, foaming
- 115 1.0% "Methocel" 4000 cps. (registered
Trade Mark) (Methyl cellulose: Dow
Chemical Midland Mich. USA)
- 1.0% Taurolin
- 23.05% Water (deionised)
- 120 19.0% Propyleneglycol
- 9.3% Glycerine

- 0.25% "Nipagin" M* (registered Trade Mark) (Methyl p-hydroxybenzoate: Nipa Laboratories Treforest, Pontypridd)
- 5 0.5% Saccharine 10% solution
1.2% Paraffin oil
1.0% Oleum menthae
2.0% "Texapon" K 12
41.7% Calcium phosphate dihydrate
- 10 * can be omitted.

Example 9

Toothpaste, foaming

- 1.0% "Methocel" 4000 cps.
1.0% Taurolin
15 21.7% Water (deionised)
19.0% Propylene glycol
9.3% Glycerine
0.5% Saccharine 10% solution
1.0% Paraffin oil
20 1.0% Oleum menthae
2.0% "Texapon" K 12
43.5% Calcium carbonate (precipitated)

Example 10

Toothpaste, foaming

- 25 33.0% Calcium carbonate (precipitated)
34.8% Water (deionised)
20.0% Glycerine
3.0% Sorbitol
2.0% "Aerosil" (registered Trade Mark) (Fine silicic acid: Degussa)
30 2.0% Texapon K 12
1.0% Oleum menthae
1.2% "Texamid" 578 L (registered Trade Mark) (Sodium Alginate: Henkel/Dehydag)
35 1.0% Paraffin oil per l
1.0% Taurolin
1.0% Saccharine 10% solution

Example 11

Mouth wash

- 40 79.0% Water (deionised)
2.0% Haurolin
1.0% "Texapon" K 12
15.0% Ethanol
45 0.5% Saccharine 10% solution
0.5% Oleum menthae
2.0% "Tween" 80 (Polyoxyethylene-sorbitan-mono-oleate: Atlas)

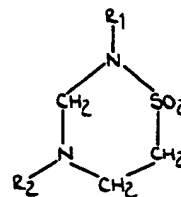
Example 12

Mouth wash

- 50 73.8% Deionised water
2.0% Taurolin
10.0% Ethanol
1.5% Parfum dentifrice 24/45 (Charabot, France)
55 0.2% Methol crystalline (Charabot, France)
5.0% Tinct. arnica
5.0% Hamamelis Extract
60 0.5% Kamillen Extract
2.0% "Texapon" K 12

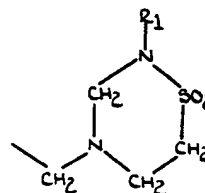
WHAT WE CLAIM IS:—

1. A dental care preparation for the treatment and/or prophylaxis of parodontosis in the form of a toothpaste, toothgel or mouthwash (as herein defined) comprising, as active ingredient, at least one compound of formula



I

[wherein R₁ represents a hydrogen atom or a straight or branched alkyl group having from one to 6 carbon atoms; and R₂ represents a hydrogen atom or a group of formula



(wherein R₁ is as defined above)].

2. A preparation as claimed in claim 1 wherein the active ingredient is bis - (1,1 - dioxo - perhydro - 1,2,4 - thiadiazinyl - 4) - methane.

3. A preparation as claimed in either of claims 1 and 2 in the form of a toothpaste or toothgel containing thickening or binding agents, humectants, foaming agents, cleansing agents, preservatives, sweetening agents, flavouring agents and/or water.

4. A preparation as claimed in either of claims 1 and 2 in the form of a mouthwash containing sweetening and flavouring agents, surfactants and/or ethanol.

5. A preparation as claimed in any of the preceding claims containing at least one further pharmacologically active ingredient.

6. A preparation as claimed in claim 5 wherein the further active ingredient is a substance active against the formation of bacterial plaque, or a substance active against caries.

7. A preparation as claimed in claim 6 wherein the substance active against the production of bacterial plaque is sodium benzoate, a high molecular polyphosphate, sodium metaphosphate, magnesium tartrate, polyvinylpyrrolidone, a polysiloxane or sodium sulphoricinoleate.

8. A preparation as claimed in claim 6 wherein the substance active against caries is a fluorine compound.

9. A preparation as claimed in any of the preceding claims for the treatment of parodon-

tosis containing from 1 to 3% by weight of the active ingredient of formula I.

10. A preparation as claimed in claim 9 which contains about 2% by weight of the active ingredient of formula I.

11. A preparation as claimed in any of claims 1 to 8 for the prophylaxis of parodontosis containing from 0.5 to 1.5% by weight of the active ingredient of formula I.

12. A preparation as claimed in claim 11 which contains about 1% by weight of the active ingredient of formula I.

13. A preparation as claimed in claim 1 substantially as herein described.

14. A preparation as claimed in claim 1 substantially as herein described in any of the Examples.

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